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Far-Advanced Pulmonary Interstitial Disease with Normal Findings on a Chest Radiograph

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DIFFUSE INTERSTITIAL LUNG DISEASE is suspected in a tachypneic patient with end inspiratory pulmonary rales and the following abnormalities of pulmonary function: reduced vital capacity, total lung capacity and diffusing capacity in the presence of normal flow rates. A radiograph of the chest usually shows diffuse interstitial abnormalities.¹ Depending on the specific disease, all measurements may not parallel one another in an individual case. For example, idiopathic interstitial fibrosis may be suspected because of abnormal findings on a routine chest radiograph, yet in such patients symptoms may not be present and results on physical examination may be within normal limits.² In contrast, patients with sarcoid may present with hilar adenopathy and normal lung parenchyma shown by chest radiograph, while pulmonary function studies usually show a decreased diffusing capacity consistent with diffuse interstitial pulmonary involvement by granuloma or fibrosis or both.³ This disparity is usually presumed to be secondary to an interstitial process undetectable by routine radiograph. However, it is not generally appreciated that, in other conditions, interstitial lung disease may occur with essentially normal findings on a chest radiograph.

Recently, we observed a young patient, with

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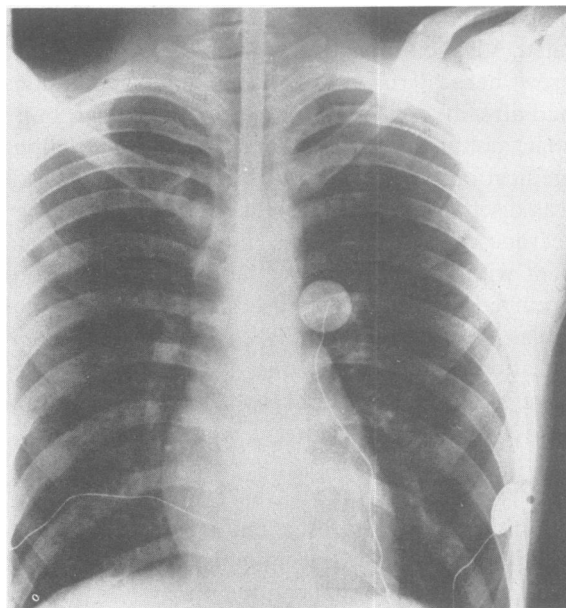


Figure 1.—Admission chest radiograph. Note clear lung fields. Diaphragm below level of 11th rib posteriorly. Gastric tube in place.

previously normal lungs, in whom there was acute onset and rapid progression of pulmonary fibrosis secondary to the ingestion of paraquat (a toxic herbicide).⁴ In this case we documented rapid progression (by pulmonary function testing) of a process compatible with severe interstitial edema or fibrosis or both while the findings on routine chest radiograph remained normal.

Report of a Case

A 16-year-old white boy ingested a mouthful of paraquat in a suicidal gesture at 8:30 a.m. He was admitted to the emergency room at 9:00 a.m. and gastric lavage with tap water and milk through a large bore gastric tube was carried out. Results of physical examination were normal except for a respiratory rate of 28 per minute. Findings on studies of blood gases (fraction of inspired oxygen [$F_{I}O_2$] 0.21) showed an arterial oxygen pressure (PaO_2) of 122 mm of mercury, an arterial carbon dioxide pressure ($PaCO_2$) of 19 mm of mercury (alveolar arterial oxygen difference [$A-aO_2$] gradient of 8 mm of mercury) and a pH of 7.56. Results of a chest radiogram (Figure 1) were normal. The therapeutic regimen, which continued throughout the patient's hospital course, was as follows: (1) low $F_{I}O_2$ to maintain his PaO_2 at approximately 50 mm of mercury (since oxygen enhances the toxicity of paraquat), (2) forced diuresis up to 10 liters per day, (3) daily

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TABLE 1.—Findings on Sequential Upright Pulmonary Function Test and Arterial Blood Gas Studies

	Hospital Day							Predicted Values	
	2	3	4	5	8	12	16		23
Vital capacity* (VC)	3.19	2.85	..	1.15	1.55	1.75	1.51	..	5.60
Alveolar volume* (V _A)	5.09	3.99	2.50	2.35	2.89	2.97	2.42	..	6.70
Diffusing capacity† (DLCO) ..	39.40	..	18.00	19.00	10.00	8.30	7.50	..	38.70
F _I O ₂	0.15	0.14	0.15	0.15	0.17	0.17	0.21	0.60	0.21
PaO ₂ ‡	51.00	46.00	48.00	48.00	42.00	44.00	44.00	50.00	>85
PaCO ₂ ‡	24.00	24.00	25.00	26.00	29.00	30.00	28.00	32.00	38-42
A-aO ₂ ‡ gradients	31.00	30.00	34.00	33.00	50.00	47.00	77.00	346.00	<10
*liters based upon height and age				F _I O ₂ =fraction of inspired oxygen					
†ml/min/mmHg				PaO ₂ =arterial oxygen pressure					
‡mmHg				PaCO ₂ =arterial carbon dioxide pressure					
				A-aO ₂ =alveolar arterial oxygen difference					

*liters based upon height and age
†ml/min/mmHg
‡mmHg

$F_{I}O_2$ =fraction of inspired oxygen
 PaO_2 =arterial oxygen pressure
 $PaCO_2$ =arterial carbon dioxide pressure
A-a O_2 =alveolar arterial oxygen difference

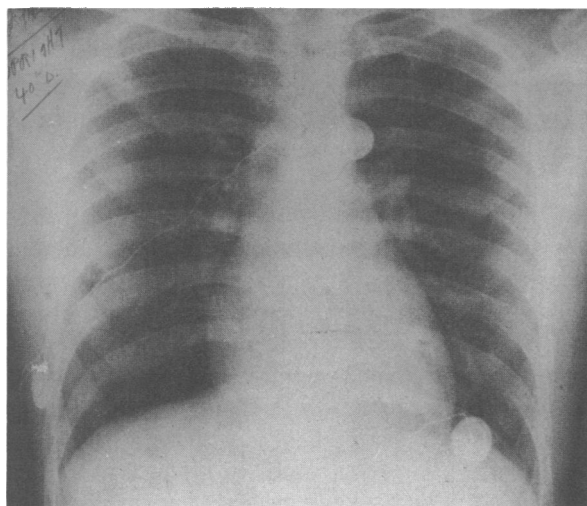


Figure 2.—Chest radiograph on fifth hospital day. Lung fields clear except for the possibility of a left sided retrocardiac infiltrate. Diaphragm above 10th rib posteriorly. Vital capacity 2.85 liters; alveolar volume 3.99 liters.

ultrafiltration hemodialysis, (4) intravenously given hydrocortisone, 1 gram daily, (5) d-propranolol and superoxide dismutase (experimental drugs which combat the toxic effects of paraquat).

The usual toxic effects associated with paraquat were seen: (1) acute renal failure, (2) hepatic involvement, (3) cardiac arrhythmias, (4) gastrointestinal irritability and bleeding.

On the second hospital day bedside upright pulmonary function studies were obtained as noted in Table 1. Both the vital capacity (VC, as determined by spirometry) and alveolar volume (V_A , as determined by neon) were 70 percent of predicted even though the single breath diffusing capacity for carbon monoxide (DLCO) was normal.⁵ By the third hospital day VC, V_A and DLCO were 50 percent of predicted. On a radiograph of the chest clear lung fields were noted

(except for a questionable retrocardiac density on the left), however, the diaphragm was elevated. By the fifth hospital day VC and V_A were 20 percent of predicted and the DLCO 50 percent of predicted. Findings on chest radiographs remained unchanged (Figure 2). In addition, during this time, the A-a O_2 gradient had increased to 30 to 33 mm of mercury (Table 1).

On the eighth hospital day alveolar infiltrates were noted in the left lower lobe by chest radiograph (Figure 3), the patient was more dyspneic and the A-a O_2 gradient was worsening (Table 1). Vigorous diuresis led to minimal improvement in the chest radiograph with concomitant increases in the VC and V_A but not the DLCO (Table 1). The patient's course was inexorably downhill as increasing amounts of supplemental oxygen were required and he died on the 22nd hospital day.

Results of a limited autopsy showed no gross pathologic alteration in any organ system except for the lungs which were described as follows: the right and left lungs weighed 1,000 grams each and were notably firm to palpation. On sectioning of the lungs, a mottled purplish-red cut surface was seen which was notably firm to palpation. On microscopic examination, diffuse, extensive, far advanced pulmonary fibrosis was found with areas of intraalveolar hemorrhage (Figure 4).

Discussion

Clinically, diffuse interstitial lung disease is suspected by findings on physical examination and pulmonary function testing, but this diagnosis is not seriously entertained unless the classic abnormalities are noted on a radiograph of the chest.² Thus, most clinicians and radiologists would seem to place undue significance on the results of a chest radiograph. Strong emphasis on

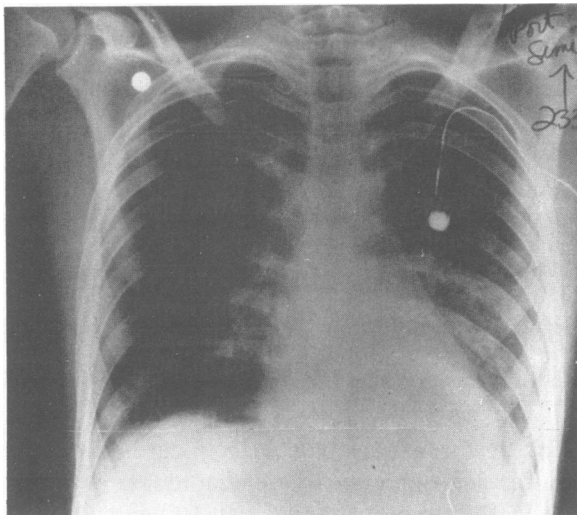


Figure 3.—Chest radiograph on eighth hospital day. Alveolar infiltrate left lower lobe. Minimal infiltrate right lower lobe. Vital capacity 1.55 liters; alveolar volume 2.89 liters; single breath diffusing capacity for carbon monoxide (DLCO) 10 ml per minute per mm of mercury.

findings from a chest radiograph may be correct in many situations, but, as shown by the present case, advanced interstitial lung disease (evidenced by typical abnormalities of pulmonary function) may only be manifested on an upright chest radiograph by elevated diaphragm. These findings are not totally unique since others have reported pulmonary fibrosis in the presence of normal findings on chest radiographs.^{6,7}

Unger and co-workers⁸ are aware of the paradox of a normal chest radiograph in patients with moderate to severe pulmonary symptoms. In a treatise dealing with hypersensitivity pneumonitis they state, "It is both surprising and disconcerting to the radiologist to be confronted with a patient with moderate to severe pulmonary symptoms without any demonstrable findings on the chest film. Because of the increasing awareness of these diseases, we will probably see more of these early patients with normal film. This fact, although well known to the allergist, does not seem to have been stressed sufficiently in the radiologic literature."

It might be argued that since we did not have tissue proof early in the course of our patient's disease (that is, when findings on chest radiographs were essentially normal while pulmonary function studies gave results compatible with severe restrictive disease) that interstitial disease was indeed not present and the decreased lung volumes shown both by radiographs and pulmo-

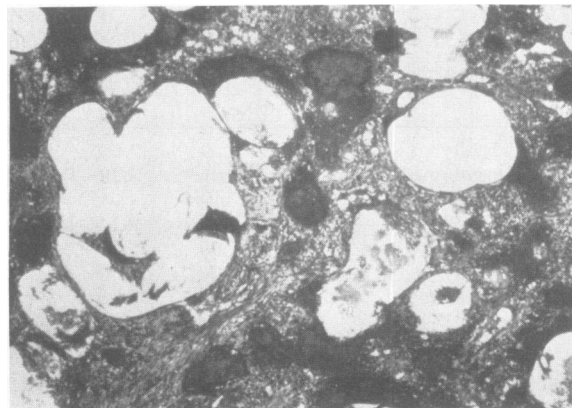


Figure 4.—Histology of the lung showing extensive, far advanced, diffuse pulmonary fibrosis.

nary function studies were due to poor patient cooperation. That this thesis is probably invalid may be surmised from several pieces of evidence: (1) The changes in lung volumes were consistently in one direction (worsening) and once they reached their minimum values tended to remain that way (Table 1). Poor patient cooperation usually produces fluctuating alterations in pulmonary functions both increasing and decreasing in a variable and unpredictable manner. Since all tests were carried out in the upright position, the effects of changes in posture on the pulmonary function tests were avoided. (2) The DLCO was much lower than would be expected just from a self-induced decrease in lung volumes. (3) The chest radiographs and pulmonary function tests, both of which showed loss of lung volume, were done at separate times during the day. Both showed changes always consistent with loss of lung volume.

In paraquat poisoning in both animals and humans, interstitial fibrosis has been noted as early as the third to fifth day after ingestion.⁹⁻¹² In our patient, changes in pulmonary function studies occurred at appropriate times.

In conclusion, our case suggests that relatively far advanced diffuse interstitial lung disease may be shown on chest radiographs only as loss of lung volumes, evident as an elevated diaphragm. In symptomatic patients in whom the diaphragm is persistently elevated with normal lung fields, pulmonary function testing may help define the clinical situation.

Summary

A case of rapidly developing and fatal pulmonary fibrosis is reported in a 16-year-old boy. At

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a time when findings on pulmonary function tests were compatible with severe interstitial lung disease, a radiograph of the chest showed clear lung fields, but elevated diaphragm. The insensitivity of routine radiographs of the chest in reflecting the pathologic changes in certain cases of far advanced pulmonary interstitial disease is underscored by this case.

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"Breath-Holding" Spells

A very common condition is the breath-holding spell which does not begin with a "holding-of-breath." This is a very poor term. Children do not hold their breath in inspiration when they have a breath-holding spell; they expire the breath and do not take a second breath. And this is very important in getting the history, because if you ask most mothers if the child holds his breath, the mother will imagine in her mind a child going "Aaah, I'm holding my breath!" when actually the child expires breath and never takes the next breath. I rarely use the term breath-holding, but will ask the mother to describe what has happened in the greatest of detail. Indeed, you will find that the child has cried or has been annoyed or in some way has been disturbed and has just stopped breathing—has not taken the next inspiration—and then turns blue. He may just pass out or may go on and have a convulsion. A convulsion with a breath-holding spell, or "not-breathing" spell, does not make it any less a breath-holding spell. Medication will not prevent that kind of convulsion. The child will convulse if he gets anoxic enough, whether or not diphenylhydantoin (Dilantin®) or phenobarbital is used, just as a child whose blood sugar drops from too much insulin will convulse, whether or not you use phenobarbital or Dilantin. These types of stresses cannot be prevented with anticonvulsant medication and should not be treated as such. The only cure I know for breath-holding spells, which are of course temper tantrums, is a very difficult one—the total ignoring of the spell.

Children never have spells without an audience and it is imperative that the mother or whomever else the child has the spells for—and it is usually a small number of people for whom a child will have breath-holding spells—leaves the room completely, without peeking through a curtain, while this episode is going on. The child has to wake up and find that he has gone through this enormous act without any audience. After one or two times, the child will invariably stop doing it. It is very difficult, however, to get parents to leave a child during a breath-holding spell.

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